

REMARKS

Claims 34, 36-47 are pending in the application. Claims 34, 37, 40, 41, 44 and 47 have been amended.

Amendments to the Claims

Claims 34, 37, 40, 41, 44 and 47 have been amended herein to correct informalities and to more particularly point out aspects of the invention. Specifically, Claim 34 has been amended to recite “carriers” rather than “carrier.” Claim 34 has been also amended to include “the first class and the second class of carriers comprise a distinct shape from each other.” The recitation of “wherein each of the carriers has at least one flat viewing surface and a shape that self-orientates the viewing surface to face a viewing direction” has been moved to be a part of the first step of the claimed method. Claim 34 has been amended to recite “coupling,” instead of “attaching,” and it also recites “contacting,” instead of “reacting.” To particularly point out aspects of the invention, the claim has been further amended to recite “the first class of carriers,” “the first vessel,” “the second class of carriers,” “the second vessel,” “randomly dispersing” and “at least a portion of the mixture.” Support for these amendments can be found throughout the Specification. Specifically, support for Claim 34 can be found at page 8, lines 1-22; FIGS. 4-9; page 33, line 30 through page 34, line 10; and page 41, line 4 through page 42, line 19.

Claim 37 has been amended to recite “at least one carrier,” instead of “each carrier.” Support for this amendment can be found in the Specification at page 28, lines 18 through 22.

Claim 40 has been amended to recite “contacting step,” rather than “reacting step.” Support for this amendment can be found in the Specification at page 8, line 16 and page 9, line 22.

Claim 41 has been amended to recite “carriers” instead of “carrier” or “particle.” Claim 41 has been also amended recite: “the first class of carriers and the second class of carriers comprise a distinct shape from each other” and “contacting the portion of the mixture with a test substance.” To particularly point out aspects of the invention, Claim 41 has been amended to recite “the imaging device,” instead of “the image device,” and to recite “the first vessel and the second vessel,” instead of “the first and second vessels.” Support for these amendments can be

found in the Specification at page 8, lines 1-22; FIGS. 4-9; page 25, line 18 through page 26, line 9; page 33, line 30 through page 34, line 10; and page 41, line 4 through page 42, line 19.

Claim 44 has been amended to recite “at least one carrier,” instead of “each carrier.” Support for this amendment can be found in the Specification at page 28, lines 18 through 22.

Claim 47 has been amended to recite “contacting step,” instead of “reacting step.” Support for Claim 47 can be found in the Specification at page 8, line 16 and page 9, line 22.

Rejection of Claims 34 and 36-47 Under 35 U.S.C. § 103(a)

Claims 34 and 36-47 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Lam *et al.* (Lam, K. S., Salmon, S. E., Hersh, E. M., Hruby, V. J., Kazmierski, W. M., Knapp, R. J., “A new type of synthetic peptide library for identifying ligand-binding activity” *Nature* 1991, 354:82-84) (hereinafter “Lam”); Egner *et al.* (Egner, B. J., Rana, S., Smith, H., Bouloc, N., Freg, J. C., Brocklesby, W. S., Bradley, M. “Tagging in combinatorial chemistry: the use of coloured and fluorescent beads” *Chem. Commun.* 1997, 735-736) (hereinafter “Egner”); U.S. Patent No. 4,053,433 (hereinafter “Lee”); Blawas *et al.*, (Blawas, A. S. and Reicher, W. M. “Protein Patterning” *Biomaterials* 1998 19:595-609) (hereinafter “Blawas”); U.S. Patent No. 6,129,896 (hereinafter “Noonan”); and U.S. Patent No. 6,210,910 (hereinafter “Walt”).

According to the Office, with respect to Claims 34 and 41, Lam discloses:

- (1) “providing a first class of carriers in a first reaction vessel and second class of carrier in second reaction vessel wherein a first type of analyte is attached to said first class of carriers, and a second type of analyte is attached to said second class of carriers” (Office Action, page 3);
- (2) “forming a mixture of carriers from the first and second vessels, the mixture having substantially equal numbers of carriers for each vessel” (Office Action, page 3);
- (3) “dispersing a portion of the mixture to an examination site on a surface, the carriers of the first and second classes being distributed to random positions across the examination site” (Office Action, pages 3-4);
- (4) “reacting the portion of the mixture with a test substance” (Office Action, page 4); and

(5) "acquiring at least one image of carriers at the examination site on the surface" (Office Action, page 4).

Furthermore, the Office states that, with respect to Claims 39 and 46, Lam discloses "covalent attachment" between the carrier and the analyte (Office Action, page 4); and with respect to Claims 40-47, Lam discloses a reaction step that occurs before the dispensing step" (Office Action, page 4).

However, the Office admits that Lam fails to teach "a first and second optically detectable code to interpret the result" and "at least one flat viewing surface and a shape that self-orient the viewing surface to face a viewing direction substantially perpendicular to the surface" (Office Action, page 4-5).

The Office further admits that Lam also fails to teach "each carrier has at least one transparent portion;" "carriers as a combination of fused fibers of various colors;" and "the attachment of biological cells to the carriers for cell identification" (Office Action, page 5).

Finally, with respect to Claim 41, the Office admits that Lam does not teach "the additional steps of acquiring a set of images at the examination site, each image corresponding to different spectral band" and using "a computer program to identify carriers of the same class by using the image to develop a mask for the carriers of the same class, and detecting one or more reporting modalities within the mask" (Office Action, page 5).

The Office asserts that the combined references of Egner, Lee, Blawas, Noonan and Walt compensate for deficiencies in Lam (Office Action, page 5); that a person of skill in the art would have been motivated to combine the references (Office Action, page 14); and one of ordinary skill in the art had a reasonable expectation of success (Office Action, page 15). The Office concludes by maintaining that the invention is obvious in view of the cited references (Office Action, page 16).

Applicants respectfully disagree. For the following reasons, the Examiner has failed to state a *prime facie* case.

The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)

noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that “rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also KSR, 550 U.S. at ___, 82 USPQ2d at 1396 (quoting Federal Circuit statement with approval).

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The Examiner’s reasoning specified above appears to fit best under the rational discussed under (G) of Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 in view of the Supreme Court Decision in *KSR International Co. V. Teleflex Inc.*

(G) Some Teaching, Suggestion, or Motivation in the Prior Art That Would Have Led One of Ordinary Skill To Modify the Prior Art Reference or To Combine Prior Art Reference Teachings To Arrive at the Claimed Invention (Emphasis added)

To reject a claim based on this rationale, Office personnel must resolve the *Graham* factual inquiries. Then, Office personnel must articulate the following:

- (1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
- (2) a finding that there was reasonable expectation of success; and
- (3) whatever additional findings based on the *Graham* factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

The rationale to support a conclusion that the claim would have been obvious is that “a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success.” *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1360, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006). If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art. *Id.*

The motivation to make the claimed invention and the reasonable expectation of success must both be found in the prior art, not the applicant's disclosure. *In re Vaeck*, 493, 20 USPQ 2d 1438, 1442 (Fed. Cir. 1991).

There is no teaching, suggestion or motivation to combine the cited references, nor is there a reasonable expectation of success

As asserted in the previous Reply to the Office Action, Applicants submit that the references of record could not be combined to arrive at the instant invention because there was no teaching, suggestion or motivation to combine the references and no reasonable expectation of success in doing so, absent the impermissible hindsight.

With respect to Claims 34 and 41, the Office admits that both Lam and Egner only disclose the use of spherical beads as carriers (see, Office Action, pages 5 and 9). The Office, however, believes that the combined references of Lee, Noonan, Blawas and Walt teach the use of other carriers with two substantially parallel planar sides instead of the round shape of a bead as described in Lam and Egner.

Applicants assert that none of Walt, Noonan, Blawas, and Lee teaches, suggests or motivates one having ordinary skill in the art to combine these references with Lam and Egner to arrive at the claimed invention, namely, the carriers in shapes that have at least one flat viewing surface and would self-orient the viewing surface to face a viewing direction, which promotes a higher degree of organization between individual carriers and preventing stacking of the carriers upon viewing.

1. Lee et al.

The Office states that flat carriers allegedly disclosed by Lee could be interpreted as the carriers having at least one flat viewing surface and a shape that self-orient the viewing surface to face a viewing direction. Applicants respectfully disagree. Such carriers suggested by Lee have tendency to form a stack by settling themselves on the top of another when distributed on a surface for viewing. This is because the carriers have a planar top and bottom side, described as "disks." During the detection stage of a multiplexed analysis, stacking of color coded carriers presents a problem, especially when two or more optically distinct signals intensify, quench, cancel or interfere with each other's optical frequency. Therefore, the microparticles disclosed by Lee, specifically in FIGS 2-5 as cited by the Examiner, are distinct from the claimed

invention. Accordingly, the microcarriers disclosed by Lee fails to provide a shape that self-orient the viewing surface to face a viewing direction. Further, Lee is silent on how to address this problem in multiplexed biochemical analysis. Thus, there is no teaching or suggestion for combining Lee with any of the cited references to arrive at Applicants' claimed invention. Nor is there reasonable expectation of success, absent a proper recognition of an existing problem.

2. Noonan et al.

The Office states that the flat chip allegedly disclosed by Noonan has at least one flat viewing surface and shape that self-orient the viewing surface to face a viewing direction. Applicants respectfully disagree. In Noonan, the bundled fibers are fused together to fix their predetermined arrangement (FIG. 3; column 4, lines 44-54). The bonded fiber bundle is then sliced into a plurality of individual devices or chips (FIG. 3; column 4, lines 44-54). Again, Noonan's carriers are similar to Lee's disk or rod carriers which fail to address the stacking problem. Noonan is also silent on solving the stacking problem. Thus, there is no teaching, suggestion or motivation to combine Noonan with any of the cited references to arrive the claimed invention.

3. Blawas et al.

Blawas describes various types of protein patterning and synthesis of such arrays. Nowhere in Blawas describes an individual carrier coupled to an analyte, which has at least one flat viewing surface and can be freely mixed with a second class of carriers, allowing the user to form a mixture of 1:1 ratio. Further, Blawas also fails to recognize the problem of stacking even though the reference discusses numerous other problems associated with protein patterning existed at the time. With respect to three dimensional protein patterning, Blawas specifically teaches away by stating that "work in the area of three-dimensional protein patterning has focused on developing components for a biological three dimensional working circuit, generally referred to as a biochip [t]he actual means for construction of such circuit are theoretical, if not speculative" (Blawas *et al.*, page 597, left column, second paragraph). There exists neither express teaching or suggestion taught by Blawas, nor motivation for a person having ordinary skill in the art to combine Blawas with any of the cited references to arrive at the claimed subject matter.

4. Walt et al.

The Office suggests that the optic fiber wells allegedly containing at least one flat surface disclosed by Walt could be interpreted as the carrier having at least one flat viewing surface and a shape that self-orient the viewing surface. Applicants respectfully disagree. The optic fiber wells disclosed by Walt are a network of fibers continuously interconnected and of a uniform size and shape. Accordingly, the fiber wells disclosed by Walt cannot be implemented in multiplexed analyses such as the one in the present invention because Claims 34 and 41 require a mixture of carriers having two different optical codes and in two distinct shapes. Thus, there is clearly no motivation to combine Walt with the cited references to arrive the claimed subject matter because Walt teaches an array of carriers far distinct from the claimed invention.

In summary, at most, Lam and Egner teach spherical beads and Lee, Noonan or Walt teaches carriers with a planar top and bottom side which present the stacking problem when they are distributed on a surface for viewing. The references are silent on solving the stacking problem because the carriers described by the cited references are designed to be implemented differently than the claimed invention. Thus, there is no teaching, suggestion or motivation to combine to arrive at the claimed subject matter. Claims 34 and 41 and their dependencies are, therefore, not *prima facie* obvious.

Furthermore, even if improperly combined, the combined references of Lam, Egner, Lee, Blawas, Noonan and Walt do not teach all elements of the claimed invention as amended as discussed below.

The combined references do not teach each and every element of the claimed invention

With respect to Claims 34 and 41 and claims dependent thereon, none of Lam, Egner, Walt, Noonan, Blawas, and Lee teaches shapes of carriers that would self-orient the viewing surface to face a viewing direction and that would allow a higher degree of organization of individual carriers and prevent stacking of the carriers upon viewing. Both Lam and Egner only disclose the use of spherical beads as carriers as noted by the Office (see, Office Action, page 5 and 9). The Office, however, believes that the combined references of Lee, Blawas, Noonan, and Walt teach the use of various other carriers with two substantially parallel planar sides instead of the round shape of a bead described in Lam and Egner. The Office cites Lee to point out disclosing examples of carriers with a planar “top” and “bottom” side (Office Action, page 9). However, such carriers have a tendency to form a stack by settling one carrier on the top of

another carrier, as discussed above. During the detection stage of a multiplexed analysis, such stacking of color coded carriers can present a serious problem.

In contrast, the Specification of the instant application particularly teaches that “shape may also play a role in how a carrier displays itself” (page 41, lines 10-11). It further identifies the problem of stacking (page 51, lines 12 and 21), and points out the advantages of well-organized compact array of carriers created by their shapes (page 51, lines 1- 30, particularly lines 21-22). The Specification also teaches that “weight distribution within a carrier also facilitates orientation” (page 51, lines 21-32). Applicants then provide an example that weight distribution within the carrier facilitates orientation: “Hemispheres will settle in a fluid with their flat surface upwards if the hemisphere is weighted on the apex of the spherical side” (page 41, lines 14-16). Furthermore, the Specification also teaches that some shapes (e.g., hexagon) can facilitate a higher degree of organization (page 51, lines 23-29). Therefore, the carrier of the claimed invention has one flat surface to face the viewing direction which promotes a lateral organization and the rest of its shape is configured to facilitate weight distribution for self-orientation optimized for viewing without creating a substantial stacking problem. None of the cited references teaches or suggests such a microcarrier. At most, Lam and Egner teach spherical beads and Lee, Noonan and Walt teach carriers with a planar top and bottom side which present the stacking issues when they are distributed for viewing on a surface. Therefore, the cited references do not teach or suggest all of the claim limitations, and thus, Claims 34 and 41 and their dependencies are not *prima facie* obvious.

Furthermore, the Office states that the combined references of Lee, Egner, Blawas, Noonan, and Walt teach “the use of a computerized sensor array for randomly detecting a mixed population of cells” (Office Action, pages 7-8). The Office states that “the identity and location of each cell type is determined by the characteristic optical response signature of the dyes or ratios of such dye” and “the apparatus for the optical detection of the cells includes instruments such as an epifluorescence microscope and CCD camera where the data is processed by a computer using image processing software” (Office Action, pages 7-8).

However, Claim 41 of the instant application specifically recites, *inter alia*, “operating a computer program to identify particles of the same class by using the images to develop a mask for the particles of the same class, and detecting one or more reporting modalities within the

mask.” None of the references of record teaches or suggests using the images to develop a mask for the particles of the same class, and detecting one or more reporting modalities within the mask. Therefore, the cited references do not teach or suggest all of the claim limitations, and thus claim 41 and its dependencies are not *prima facie* obvious.

Furthermore, the instant application teaches that “shapes may be combined with colors to improve diversity. . . . [a]vailable indicia from one class may be combined with indicia from other classes to further broaden the coding vocabulary” (page 42, lines 13-16). To that end, FIGS 4-9 depict a mixture of carriers with at least two different shapes and two different classes of analytes.

Claims 34 and 41, as amended, require two distinct classes of carriers with distinct optical codes and distinct shapes. None of the cited references teaches a mixture of the first and second classes of carriers having a distinct optical code as well as a distinct shape from each other. Therefore, Applicants assert that Claim 34 and 41, as amended, are not obvious in view of the cited references because the references of record do not teach all elements of the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 34 and 36-47 Under 35 U.S.C. § 112, Second Paragraph

Claims 34 and 36-47 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. According to the Office, Claims 34 and 41 are rejected because the claim limitation “the code” is indefinite for lacking proper antecedent basis. Claims 34 and 41 have been amended to delete the phrase, “wherein the code exists throughout the structure of the carrier,” thereby rendering the rejection moot.

Claim 38 is rejected for lacking antecedent basis for “the coupling step.” Applicants have amended Claim 34 from which Claim 38 is dependent on to recite “coupling,” instead of “attaching,” to provide sufficient antecedent basis for Claim 38.

Claim 41 is rejected for lacking antecedent basis for “the image device.” Claim 41 has been amended to recite “the imaging device,” which has antecedent basis in Claim 41.

Claim 47 is rejected for lacking antecedent basis for “the reacting step.” Claim 47 has been amended to recite “the contacting step,” which has antecedent basis in Claim 41, as amended.

Reconsideration and withdrawal of the rejection are respectfully requested.

Supplemental Information Disclosure Statement

A Sixth Supplemental Information Disclosure Statement (IDS) is being filed concurrently herewith. Entry of the Sixth Supplemental IDS is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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